

REMARKS/ARGUMENTS

Claims 1 to 5 are pending in this application and stand finally rejected as follows:

- (1) claims 1 to 5 stand rejected under 35 U.S.C. § 112, second paragraph;
- (2) claims 1 to 5 stand rejected under 35 U.S.C. § 102(b) over US-A-5,461,146;
- (3) claims 1 to 5 stand rejected under 35 U.S.C. § 103(a) over US-A-5,461,146; and
- (4) claims 1 to 5 stand rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1 to 4 of US-B-6,306,849.

Applicants are herein amending claim 1.

Amendments

Applicants are herein amending claim 1 to eliminate SR^{27B} as a possible R⁷ group in $-(CH_2)_kR^7$ of Formula I [See substituent e)].

Applicants are also herein amending claim 1 to specify the substituents of various moieties of Formula I, specifically that:

- said substituted aryl, said substituted heteroaryl, said substituted aralkyl, or said substituted arylaminocarbonyl comprises 1 to 3 independent substitutions selected from the group consisting of lower alkyl, hydroxy, lower alkoxy, carboxyl, lower alkoxy carbonyl, nitro, amino, mono-lower alkylamino, di-lower alkylamino, and halo; and
- substituted lower alkyl, said lower alkoxy, said substituted lower alkoxy carbonyl, and mono-lower alkylamino or di-lower alkylamino comprises 1 to 3 independent substitutions selected from the group consisting of hydroxy, lower alkoxy, carboxyl, lower alkoxy carbonyl, nitro, amino, mono-lower alkylamino, di-lower alkylamino, dioxolane, dioxane, dithiolane, and dithione.

Support for the amendment may be found in the specification, *inter alia*, on, for example, page 7, lines 26 to 29, where the term “substituted” as it is used with respect to a “lower alkyl” group is defined to include one to three independently-selected substituents, such as hydroxy, lower alkoxy, carboxyl, lower alkoxy carbonyl, nitro, amino, mono- or di-lower

alkylamino, dioxolane, dioxane, dithiolane, and dithione. See also, page 7, line 32 to page 8, line 2, where the term “substituted” as it is used with respect to “aryl,” “heteroaryl,” and “aralkyl” groups is defined to include one to three independently-selected substituents, such as lower alkyl, hydroxy, lower alkoxy, carboxy, lower alkoxycarbonyl, nitro, amino, mono- or di-lower alkylamino, and halogen.

Applicants are also herein amending claim 1 to specify that the heteroaryl group is pyridyl, pyrimidyl, pyrrolyl, furyl, thienyl, imidazolyl, triazolyl, tetrazolyl, quinolyl, isoquinolyl, benzoimidazolyl, thiazolyl or benzothiazolyl. Support for the amendment may be found in the specification, *inter alia*, on, for example, page 7, lines 22 to 25.

Further, applicants are herein amending claim 1 to specify that in substituent X of Formula I the α -amino acid (in which the hydroxyl group of the carboxyl group is excluded) is glycine, alanine, proline, glutamic acid or lysine. Support for the amendment may be found in the specification, *inter alia*, on page 8, lines 7 to 9.

In addition, applicants are herein amending claim 1 to specify that the heterocyclic groups formed from either R⁵ and R⁶ or R²³ and R²⁴, when they are combined with the nitrogen atom to which they are attached, are pyrrolidinyl, piperidinyl, piperidino, morpholinyl, morpholino, thiomorpholino, N-methylpiperazinyl, indolyl, or isoindolyl. Support for the amendment may be found in the specification, *inter alia*, on page 8, lines 5 to 7.

Applicants submit that the amendments to the claims do not introduce new matter and are fully supported by the specification and claims, as originally filed. Applicants request the Examiner to enter the amendment under 37 C.F.R. § 1.116(b) because the amendments to the claims either cancel claims, comply with requirements of form expressly set forth in a previous Office Action, or present the rejected claims in better form for consideration on appeal.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1 to 5 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants respectfully traverse the rejection because the pending claims, as amended, are clear and definite:

(ii) The Office Action continues to allege that the term “substituted” as used in the claims is indefinite. Applicants respectfully traverse the rejection and submit that the term “substituted” is clearly defined in the specification and that one skilled in the art would understand the scope and meaning of the term as it is used in the claims when read in light of the specification. See, for example, page 7, lines 26 to 29, where the term “substituted” as it is used with respect to a “lower alkyl” group is defined to include one to three independently-selected substituents, such as hydroxy, lower alkoxy, carboxyl, lower alkoxycarbonyl, nitro, amino, mono- or di-lower alkylamino, dioxolane, dioxane, dithiolane, and dithione. See also, page 7, line 32 to page 8, line 2, where the term “substituted” as it is used with respect to “aryl,” “heteroaryl,” and “aralkyl” groups is defined to include one to three independently-selected substituents, such as lower alkyl, hydroxy, lower alkoxy, carboxy, lower alkoxycarbonyl, nitro, amino, mono- or di-lower alkylamino, and halogen.

The proper inquiry, when determining whether a claim satisfies the requirements of 35 U.S.C. § 112, second paragraph, is a determination “whether those skilled in the art would understand what is claimed when the claim is read in light of the specification.” *Orthokinetics Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986). Thus, if those skilled in the art can understand what is claimed when the claim is read in light of the specification, a rejection under 35 U.S.C. § 112, second paragraph, is inappropriate. The present specification describes chemical moieties that may be unsubstituted or substituted. Those of skill in the art of synthetic organic chemistry, armed with the specification, would recognize what groups may be substituents on lower alkyl, aryl, heteroaryl, and aralkyl, as described above.

While applicants are not conceding that the terminology is unclear, in an effort to expedite prosecution, applicants are herein amending claim 1 to incorporate the substituents for each moiety directly into the claim, thus rendering moot the indefiniteness rejection with respect to the terminology. Accordingly, applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

(iii) The Office Action continues to allege that the term “heteroaryl” as used in the claims is indefinite. Applicants respectfully traverse the rejection and submit that the term “heteroaryl” is clearly defined in the specification and that one skilled in the art would understand the scope and meaning of the term as it is used in the claims, when read in light of the specification, including the number and type of heteroatoms present, ring size and number of rings. See, for example, page 7, lines 22 to 25 where the term “heteroaryl” moiety is defined to include at least one hetero atom selected from O, S, and N, and include pyridyl, pyrimidyl, pyrrolyl, furyl, thienyl, imidazolyl, triazolyl, tetrazolyl, quinolyl, isoquinolyl, benzoimidazolyl, thiazolyl and benzothiazolyl. Applicants submit that one skilled in the art would have no difficulty understanding what moieties are meant to be encompassed by the term as it is generally known in the art. See, for example, the definitions provided by the IUPAC (submitted with previous response).

While applicants are not conceding that the terminology is unclear, in an effort to expedite prosecution, applicants are herein amending claim 1 to incorporate the substituents for each moiety directly into the claim, thus rendering moot the indefiniteness rejection with respect to the terminology. Accordingly, applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

(iv) The Office Action continues to allege that the term “heterocyclic” is indefinite. While applicants are not conceding that the terminology is unclear, in an effort to expedite prosecution, applicants are herein amending claim 1 to specify the heterocyclic group is pyrrolidinyl, piperidinyl, piperidino, morpholinyl, morpholino, thiomorpholino, N-methylpiperazinyl, indolyl, or isoindolyl, thus rendering moot the indefiniteness rejection

with respect to the terminology. Accordingly, applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

(vi) The Office Action continues to allege that the definition of “NR²³R²⁴” as “the residue of an α -amino acid in which the hydroxyl group of the carboxyl group is excluded” is unclear with respect to which amino acids are intended. While applicants are not conceding that the terminology is unclear, in an effort to expedite prosecution, applicants are herein amending claim 1 to specify the α -amino acids, thus rendering moot the indefiniteness rejection with respect to the terminology.

Applicants respectfully submit that the claims, as amended, are not indefinite and particularly point out and distinctly claim the subject matter that applicants regard as the invention. Thus, applicants respectfully request withdrawal of the rejection of pending claims under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102(b)

Claims 1 to 5 are rejected under 35 U.S.C. § 102(b) as anticipated by US-A-5,461,146 (*Lewis*). Claim 1 requires that R¹ or R² be selected from:

- a) $-\text{CO}(\text{CH}_2)_j\text{R}^4$;
- b) $-\text{CH}(\text{OH})(\text{CH}_2)_b\text{R}^{4A}$;
- c) $-(\text{CH}_2)_d\text{CHR}^{31}\text{CO}_2\text{R}^{32}$;
- d) $-(\text{CH}_2)_d\text{CHR}^{31}\text{CONR}^5\text{R}^6$;
- e) $-(\text{CH}_2)_k\text{R}^7$;
- f) $-\text{CH}=\text{CH}(\text{CH}_2)_m\text{R}^{12}$;
- g) $-\text{CH}-\text{C}(\text{CO}_2\text{R}^{33A})_2$;
- h) $-\text{C}\equiv\text{C}(\text{CH}_2)_n\text{R}^{13}$; and
- i) $-\text{CH}_2\text{OR}^{44}$.

The *Lewis* reference does not disclose any compounds that meet all of the requirements of claims 1 to 5, as amended. Contrary to the assertion that Compound II-47 of *Lewis*

anticipates claim 1 because it reads on $-\text{CH}_2\text{OR}^{44}$, applicants wish to point out that R^1 in Compound II-47 is $-\text{CH}_2\text{OC}_2\text{H}_5$ and thus contains an unsubstituted alkyl, whereas R^{44} of claim 1 requires a substituted alkyl group, where the substituted lower alkyl has 1 to 3 independent substitutions selected from the group consisting of hydroxy, lower alkoxy, carboxyl, lower alkoxy carbonyl, nitro, amino, mono-lower alkylamino, di-lower alkylamino, dioxolane, dioxane, dithiolane, and dithione. Applicants respectfully submit that the *Lewis* reference does not anticipate the compounds of claims 1 to 5. Accordingly, applicants request withdrawal of the rejection of claims 1 to 5 under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

Claims 1 to 5 stand rejected under 35 U.S.C. § 103(a) as obvious over US-A-5,461,146 (*Lewis*). Applicants respectfully traverse because *Lewis* does not disclose, teach, or suggest the requisite elements of applicants' claimed invention, as defined in claims 1 to 5. Specifically, *Lewis* fails to disclose, teach, or suggest any compounds where R^1 or R^2 is selected from:

- a) $-\text{CO}(\text{CH}_2)_j\text{R}^{44}$;
- b) $-\text{CH}(\text{OH})(\text{CH}_2)_b\text{R}^{4A}$;
- c) $-(\text{CH}_2)_d\text{CHR}^{31}\text{CO}_2\text{R}^{32}$;
- d) $-(\text{CH}_2)_d\text{CHR}^{31}\text{CONR}^{5}\text{R}^6$;
- e) $-(\text{CH}_2)_k\text{R}^7$;
- f) $-\text{CH}=\text{CH}(\text{CH}_2)_m\text{R}^{12}$;
- g) $-\text{CH}-\text{C}(\text{CO}_2\text{R}^{33A})_2$;
- h) $-\text{C}\equiv\text{C}(\text{CH}_2)_n\text{R}^{13}$; and
- i) $-\text{CH}_2\text{OR}^{44}$.

With the exception of moiety (e) above, there is no evidence or reasoning presented in the Office Action of why any of the other R^1 or R^2 moieties would be obvious in view of the teaching of *Lewis*. There has been no evidence presented that would indicate the functional equivalence of the R^1 or R^2 moieties with those disclosed in *Lewis*, except allegedly with respect to moiety e). With respect to moiety (e), it is alleged that the only difference between

moiety e) and Compound II-30 of *Lewis* is the length of the alkylene linker in $-(CH_2)_kR^7$. Applicants are herein amending claim 1 to eliminate SR^{27B} as a possible R^7 group in $-(CH_2)_kR^7$ of Formula I, thereby rendering moot the rejection with respect to Compound II-30.

Applicants respectfully submit that the *Lewis* reference as a whole does not provide any suggestion of the desirability of doing what the inventor has done. "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). Homology involves close structural similarity which must be considered with all other relevant facts in determining the issue of obviousness. *In re Mills*, 281 F.2d 218, 126 USPQ 513 (CCPA 1960); *In re Wiechert*, 370 F.2d 927, 152 USPQ 247 (CCPA 1967). As expressed in MPEP § 2144.09, homology should not be automatically equated with *prima facie* obviousness because the claimed invention and the prior art must each be viewed "as a whole." *In re Langer*, 465 F.2d 896, 175 USPQ 169 (CCPA 1972) (Claims to a polymerization process using a sterically hindered amine were held unobvious over a similar prior art process because the prior art disclosed a large number of unhindered amines and only one sterically hindered amine (which differed from a claimed amine by 3 carbon atoms), and therefore the reference as a whole did not apprise the ordinary artisan of the significance of hindered amines as a class.).

Applicants respectfully submit that the *Lewis* reference, viewed as a whole, does not expressly or impliedly suggest the claimed invention nor would a artisan find the claimed invention obvious in light of *Lewis*. Thus, applicants respectfully submit that *Lewis* does not render obvious applicants' claimed invention. Accordingly, applicants request withdrawal of the rejection of claims 1 to 5 under 35 U.S.C. § 103(a).

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PATENT
REPLY FILED UNDER EXPEDITED
PROCEDURE PURSUANT TO
37 C.F.R. § 1.116

Obviousness-Type Double Patenting Rejection

Claims 1 to 5 are rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1 to 4 of US-B-6,306,849. Applicants request that this rejection be held in abeyance until the identification of allowable subject matter, at which time applicants will consider submitting a terminal disclaimer to obviate the rejection.

Conclusions

Applicants request:

- (1) entry of the amendment to the claims; and
- (2) reconsideration and withdrawal of the rejection of the claims; and
- (3) allowance of claims 1 to 5.

If the Examiner is of a contrary view, the Examiner is requested to contact the undersigned attorney at (215) 557-3861.

Respectfully submitted,


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